

Responsivity to dyslexia training indexed by the N170 amplitude of the brain potential elicited by word reading

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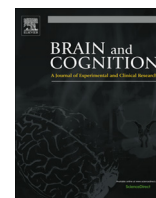
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Responsivity to dyslexia training indexed by the N170 amplitude of the brain potential elicited by word reading



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ABSTRACT

The present study examined training effects in dyslexic children on reading fluency and the amplitude of N170, a negative brain-potential component elicited by letter and symbol strings. A group of 18 children with dyslexia in 3rd grade (9.05 ± 0.46 years old) was tested before and after following a letter-speech sound mapping training. A group of 20 third-grade typical readers (8.78 ± 0.35 years old) performed a single time on the same brain potential task. The training was differentially effective in speeding up reading fluency in the dyslexic children. In some children, training had a beneficial effect on reading fluency ('improvers') while a training effect was absent in others ('non-improvers'). Improvers at pre-training showed larger N170 amplitude to words compared to non-improvers. N170 amplitude decreased following training in improvers but not in non-improvers. But the N170 amplitude pattern in improvers continued to differ from the N170 amplitude pattern across hemispheres seen in typical readers. Finally, we observed a positive relation between the decrease in N170 amplitude and gains in reading fluency. Collectively, the results that emerged from the present study indicate the sensitivity of N170 amplitude to reading fluency and its potential as a predictor of reading fluency acquisition.

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1. Introduction

Dyslexia is a specific reading disability characterized by dysfluent and inaccurate word recognition, spelling and phonological decoding (Lyon, Shaywitz, & Shaywitz, 2003). Reading dysfluency is one of the most persistent symptoms of developmental dyslexia (Shaywitz & Shaywitz, 2008). Fluent readers are able to develop visual expertise for fast and automatic identification of words, whereas dyslexic readers persistently fail to acquire fluent reading.

Neuroimaging studies identified two posterior neural systems, primarily in the left hemisphere, that are particularly important for the development of reading skills (Schlaggar & McCandliss,

2007). The first system is located in the left dorsal temporo-parietal region and relates to phonological processing and cross-modal integration of letters and speech sounds (Blomert, 2011; Van Atteveldt, Formisano, Goebel, & Blomert, 2004). The second system is located in the ventral left occipito-temporal region and involves areas in the middle and inferior temporal and occipital gyrus. Within this system the area located at the left lateral occipito-temporal sulcus has been called the "visual word form area" (VWFA) because of its suggested specialization for printed word recognition (Dehaene & Cohen, 2011; McCandliss, Cohen, & Dehaene, 2003).

Longitudinal studies suggested a model assuming that the left dorsal temporo-parietal system develops at the first stages of reading acquisition when letter-speech sound mappings are established, and later supports the specialization of the visual system for word recognition (McCandliss & Noble, 2003; Sandak, Mencl, Frost, & Pugh, 2004). Importantly, dysregulation of both the temporo-parietal and occipito-temporal systems have

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been found in dyslexics (Blau et al., 2010; Brunswick, McCrory, Price, Frith, & Frith, 1999; Helenius, Tarkiainen, Cornelissen, Hansen, & Salmelin, 1999; Paulesu et al., 2001; Shaywitz & Shaywitz, 2008; Simos, Breier, Fletcher, Bergman, & Papanicolaou, 2000; Žarić et al., 2014).

1.1. Current study

The current study is concerned with the specialization of the occipito-temporal system associated with increasing reading fluency. Behavioral indices of reading fluency will be augmented by recording brain potentials associated with visual word recognition. The brain potential of interest is N170, an early brain potential component related to visual processing of print. N170 has a negative polarity and peaks around 200 ms after stimulus onset. N170 has been related previously to various forms of general visual expertise (Tanaka & Curran, 2001). Most interestingly, however, N170 has been shown to be sensitive to orthographic processing and its sources have been localized in the VWFA (Dien, 2009; Rossion, Joyce, Cottrell, & Tarr, 2003). In literate individuals, larger N170 amplitudes are found for words compared to strings of symbols, shapes or dots (Bentin, Mouchetant-Rostaing, Giard, Echallier, & Pernier, 1999; Maurer, Brem, Bucher, & Brandeis, 2005). Moreover, N170 responses appear to be sensitive to word similarity, being larger to letter-like stimuli (e.g., pseudofonts) compared to stimuli matched on low-level features (Bentin et al., 1999; Eulitz et al., 2000; Schendan, Ganis, & Kutas, 1998; Tarkiainen, Helenius, Hansen, Cornelissen, & Salmelin, 1999).

In a series of brain potential studies, Maurer and colleagues examined N170 amplitude differences to words vs. strings of icon-like symbols at different stages of reading acquisition in both typical readers and dyslexics (Maurer & McCandliss, 2007; Maurer et al., 2011). The data of typical readers indicated a significant left-lateralized N170 tuning effect that remains relatively stable during the first years of reading acquisition (Maurer et al., 2005). The N170 word-symbol differences in typically reading children were larger for 2nd grade children relative to kindergartners, but leveled off between 2nd grade and 5th grade (Maurer et al., 2011). This pattern of findings was taken to suggest an inverted “U” model of development of visual expertise, in which perceptual learning is critically important during the first two or three years of learning to read and then gradually declines as expertise develops. In the same series of studies, the dyslexic children in 2nd grade showed a reduced word vs. symbol difference in N170 amplitude as compared to normal readers. The authors interpreted the reduced word-symbol difference in dyslexics as a lack of visual specialization for print, reflecting a deficit in expertise for rapid word recognition. Related brain potential studies suggested, however, that the N170 difference between dyslexic and typical readers continues to persist in pre-adolescents (Araújo, Bramão, Faísca, Petersson, & Reis, 2012) and adulthood (Helenius et al., 1999; Mahé, Bonnefond, Gavens, Dufour, & Doignon-Camus, 2012). Moreover, Fraga González et al. (2014) reported a smaller N170 to words at the left vs. right hemisphere sites in typical readers that was absent in dyslexics. The latter observation was interpreted to suggest that visual decoding of words requires less effort in typical compared to dyslexic readers.

The primary goal of the present study was to examine whether a dyslexia training that purportedly increases reading fluency would alter N170 amplitude to words in dyslexic children. For this purpose, we examined a group of dyslexic children following a training expected to improve reading fluency in a relatively short period of time (around 5 months). The current training is an adaptation of an intervention program previously shown to have beneficial effects on reading fluency (Tijms, 2007). The

training is inspired by a rapidly growing body of research suggesting a letter-speech sound binding deficit as the most proximal cause for dyslexia (e.g., Blau et al., 2010; Blomert, 2011). The training provides for systematic practice on regular and irregular letter-speech sound mappings at increasing levels of complexity, and its focus is on attaining automated letter-speech sound integration. Importantly, the focus of the training is not only on learning of letter-speech sound correspondences, but also emphasizes intensive exposure fostering automation of these associations.

The beneficial effects of the current training on reading fluency were evaluated in detail in a previous study (Fraga González et al., 2015). The primary aim of the current study was to assess whether the beneficial effects of the training on reading fluency are paralleled by a normalization of the dyslexic N170 amplitude pattern to the left-lateralized N170 amplitude pattern for word reading that we observed in typical readers in a previous brain potential study (Fraga González et al., 2014). In this study, we examined N170 amplitudes associated with word recognition in dyslexic and typical readers in 3rd grade. The analysis of N170 amplitudes showed smaller N170 amplitudes to words at the left vs. right hemisphere site in typical readers. This hemispheric difference in N170 amplitude was absent in dyslexic children. In view of the anticipated reading-fluency gains, we predicted the N170 amplitude lateralization pattern to normalize in our dyslexic sample after training; that is, N170 amplitude should decrease over the left compared to the right hemisphere (Fraga González et al., 2014).

A second goal of the present study was to evaluate training responsiveness. It is estimated that around 2–6% of poor readers following special interventions in 1st or 2nd grade will remain having reading difficulties (Torgesen, 2000). Few brain potential studies related brain activity in dyslexics to intervention outcomes. Molfese and co-workers, using a visual word rhyming task, reported larger normalization of N170 and P1 amplitudes in 2nd grade responders but not in poor responders (Molfese, Fletcher, & Denton, 2013). This was supported by a MEG study showing occipito-temporal under activation in poor responders (Rezaie et al., 2011a). A more complex pattern of normalizing in responders, and compensatory changes in brain activity in poor responders was reported in another MEG study in children (Simos et al., 2007). In addition, another study reported that brain potentials (particularly in the 400–600 ms time window) to letter sound matching predicted reading gains after a short intervention in first-grade children (Lemons et al., 2010). Finally, Hasko and colleagues observed that fronto-temporal brain potentials in a phonological decision task were associated with intervention gains in third grade dyslexics (Hasko, Groth, Bruder, Bartling, & Schulte-Körne, 2014). The brain potential findings, currently available, led us to predict that the N170 would differentiate between responders vs. non-responders to the training focusing on improving reading fluency.

In brief, the aims of the present study were twofold. First, we will examine the N170 amplitude changes associated with a training designed to increase reading fluency in dyslexic children. We expect that after attaining higher levels of reading fluency, the N170 amplitude pattern in dyslexics will change towards the lateralized pattern previously observed in typical readers (Fraga González et al., 2014). Secondly, we will examine whether N170 amplitude changes associated with training will discriminate between improvers (i.e., dyslexics showing a beneficial effect of training on reading fluency), vs. non-improvers, (i.e., dyslexics showing no benefits). In this context, we will also assess whether N170 amplitude at pretest discriminates between improvers and non-improvers. If so, N170 amplitude may qualify as a neural marker for treatment sensitivity.

Table 1
Descriptive statistics of reading accuracy and fluency scores.

	Typical Readers	Dyslexics	ANOVA		
	<i>M</i> (<i>SD</i>)	<i>M</i> (<i>SD</i>)	<i>F</i>	<i>p</i> -value	η^2
<i>N</i>	20	18			
Sex ratio (m:f)	8:12	8:10			
Handedness (L:R) ^a	2:15	3:15			
Age	8.78 (0.35)	9.05 (0.46)	4.03	0.064	0.10
Raven (IQ) ^b	7.04 (1.49)	7.45 (1.44)	0.74	0.416	0.02
<i>3DM Word reading - accuracy^c</i>					
High frequency	99.12 (1.12)	92.02 (7.20)	18.97	0.000	0.34
Low frequency	97.25 (3.23)	82.96 (16.54)	14.37	0.001	0.28
Pseudowords	87.37 (9.65)	70.72 (16.37)	14.94	0.000	0.29
Total [T] ^d	49.50 (9.06)	32.33 (12.76)	23.23	0.000	0.39
<i>3DM Word reading - fluency [T]</i>					
High frequency	52.95 (7.58)	30.50 (5.43)	107.87	0.000	0.75
Low frequency	54.65 (9.02)	31.11 (6.46)	83.83	0.000	0.70
Pseudowords	53.00 (9.44)	30.78 (5.55)	75.96	0.000	0.68
Total	53.95 (9.34)	29.83 (5.53)	91.10	0.000	0.72
One-Minute Test -fluency [SS] ^e	11.55 (2.82)	3.44 (1.82)	108.04	0.000	0.75
Text reading - fluency [T] ^f	54.70 (8.04)	33.11 (5.66)	89.71	0.000	0.71
<i>Letter-speech sound associations [T]</i>					
LSS identification - accuracy	46.95 (7.70)	43.83 (13.27)	0.80	0.416	0.02
LSS discrimination - accuracy	50.20 (9.25)	45.72 (8.59)	2.37	0.154	0.06
LSS identification - fluency	52.80 (7.08)	46.00 (7.06)	8.76	0.006	0.20
LSS discrimination - fluency	51.10 (8.01)	51.83 (8.92)	0.07	0.791	0.00
3DM spelling - accuracy	50.60 (9.14)	36.11 (8.34)	25.84	0.000	0.42
3DM spelling - fluency	54.55 (8.70)	40.61 (8.30)	25.40	0.000	0.41
Phoneme deletion -accuracy [T] ^f	52.70 (7.63)	39.06 (9.39)	23.78	0.000	0.40
<i>3DM naming speed scores [T]^f</i>					
Letters	50.05 (7.13)	37.53 (7.71)	26.33	0.000	0.43
Numbers	50.65 (10.92)	36.53 (8.58)	18.62	0.000	0.35
Total	49.85 (7.91)	35.18 (9.31)	26.89	0.000	0.43

Note. LSS = Letter-speech sound.

False Discovery Rate (FDR) correction for multiple comparisons was applied to the *p* values.

^a Data missing for 3 participants; Typical *n* = 17.

^b C scores (*M* = 5, *SD* = 2).

^c Raw scores.

^d T scores (*M* = 50, *SD* = 10).

^e SS scores (*M* = 10, *SD* = 3).

^f Data missing for one participant; Dyslexics *n* = 17.

2. Methods

2.1. Participants

Third-grade dyslexic children (*N* = 18; 9.05 ± 0.46 years old) were recruited from a nation-wide center for dyslexia in the Netherlands.² The initial sample size for this group was 22 children. Two children did not take part in the posttest ERP recordings and data from two children was discarded due to technical problems during recording. Some behavioral measures are missing due to computer failure (see footnotes in Table 1). All participants had a percentile score of 10 or lower on a standard reading test. A group of 20 third-grade typical readers (8.78 ± 0.35 years old) was recruited from several primary schools attended by children with the same socio-demographical background as the dyslexic group (see Table 1 for group characteristics). None of the typical readers had a history of reading difficulties and all had a percentile score of 25 or higher on standard reading tests (see Section 2.3). The group of typical readers did not take part in the letter-speech sound training. All children were native Dutch speakers, received two and a half years of formal reading instruction in primary education. Children with below average IQ (*IQ* < 85 on a non-verbal IQ-test), uncorrected

sight problems, hearing loss, diagnosis of ADHD or other neurological or cognitive impairments were excluded. The Ethics Board of the University of Amsterdam approved this research. All parents or caretakers signed informed consent.

2.2. Procedure

The present study used a pretest-training-posttest design. The dyslexic children took part in an extensive differential diagnostic assessment before and after training. They received an average of 33.83 ± 0.51 training sessions (see Section 2.4). The average number of weeks between pre- and posttest for the behavioral assessments was 23.11 ± 3.39 weeks and for the brain potential recordings it was 22.00 ± 2.85 weeks. The number of weeks elapsing between pre- and posttest did not significantly differ between behavioral and brain potential measurements, $p = 0.109$. The measurements of typical readers took place within a period of around 3 months following the pretest measurements in the dyslexic readers. The mean (*SD*) number of weeks elapsed between the measurements of typical readers and dyslexics at pretest was 10.15 (2.39).

2.3. Behavioral assessment

A series of tests was used to assess the reading skills of the participants. The children took the tests at their school. Test scores at the pretest are presented in Table 1.

² The participants of the current study were included as part of a larger sample in our behavioral study assessing treatment effects on reading. Further, the group of typical readers, used as a baseline in the present study, participated in a previous ERP study (Fraga González et al., 2014).

Word reading skills were measured using a Dutch version of the *One-minute test* (*Een-Minut-Test*, EMT; Van den Bos, Spelberg, Scheepsmas, & De Vries, 1999), a time-limited test consisting of a list of 116 unrelated words of increasing difficulty. The number of correctly read words within 1 min serves as reading fluency score. Text reading fluency was assessed also by presenting a coherent text of increasing difficulty. The children were asked to read the story out loud within 1 min (*Schoolvaardigheidstoets Technisch Lezen*; De Vos, 2007). In addition, the 3DM battery of tests (test reliability information available in *Dyslexia Differential Diagnosis*; 3DM, Blomert & Vaessen, 2009) was individually administered. The scores of the following 3DM subtests were used. The *Word Reading task* contains visually presented high-frequency words, low-frequency words and pseudowords. Accuracy (% correct) and fluency (correct words in 1 min) were measured. The *Rapid Automatized Naming* (RAN) consists of blocks of letters or numbers that are presented visually and have to be read as fast and accurately as possible. Fluency is the time in seconds needed to name a screen of 15 items. The *Letter-Speech Sound (LSS) association tasks* consist of identification and discrimination tasks. In the identification task an aurally presented speech sound has to be matched to one out of four visually presented letters. In the discrimination task the child has to judge whether the speech sound and letter on the screen are congruent or incongruent. The *Computerized Spelling task* consists of words that are presented both aurally and visually. The visual words are displayed on screen with missing letters. Participants have to select the missing letter out of four alternatives. For the last two subtests, accuracy (% correct) as well as response time (sec/item) is measured.

Finally, the *RAVEN Coloured Progressive Matrices* was used to obtain an estimate of fluid IQ (RAVEN CPM; Raven, Raven, & Court, 1998) and the *Child Behavior Checklist* (CBCL) was completed by the parents to exclude any additional behavioral problems (Achenbach et al., 2008).

2.4. Training

Dyslexic children were provided with an intensive tutor and computer-assisted training program. Well-instructed junior psychologists provided the one-to-one training during 45-min sessions. The training frequency was two sessions per week.

The training was constructed in accordance with general skill acquisition paradigms (Davydov, 1995; Schneider, 2003), which basically implies that each (letter-speech sound) element is taught explicitly at first and consequently repeated intensively in order to obtain a transition from accurate, controlled to associative, automatic processing. In a previous study, we showed that massive exposure to letter-speech sound correspondences is substantially more effective in automatizing letter-speech sound integration when it is preceded by explicit teaching of these correspondences than when it is presented on its own (Aravena, Snellings, Tijms, & van der Molen, 2013). Sessions consist therefore of instruction followed by practice.

During instruction, letter-speech sound correspondences are explicitly trained (first regular and subsequently irregular correspondences), aiming at a step-by-step accurate mastery of the learned associations. The tutor explains the letter-speech sound correspondences to the participant by presenting phonemes both in isolation as within the context of a (visual) word. Then, the child has to identify the phoneme type (e.g., 'long vowel'), syllable type (e.g. 'stressed syllable') and operating rule (e.g. 'delete a phoneme if the terminal phonic element of a syllable belongs to a certain category'), both orally and by pressing the corresponding buttons in the touch screen. The child receives on-screen feedback as well as from the tutor. During practice, the computer training provides a high exposure to the specific letter speech sound associations

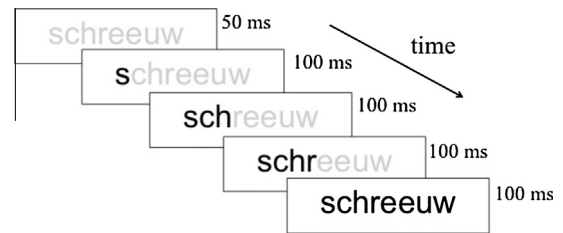


Fig. 1. Example of a practice item from the reading training based on letter-speech sound mapping. The presentation of the word *schreeuw* [sxre:u] (English: shout) under time-demanding conditions. The visual presentation is sound by sound: s[s] – ch[x] – r[r] – eeuw[e:u]. (IPA symbols in brackets).

that were taught during instruction to stimulate the automatic integration of letters and speech sounds.

A typical example of an exercise during practice consists of the projection of individual words, speech sound by speech sound, on the computer screen under (progressive) time demands (see Fig. 1). The child is asked to pronounce the word sound by sound (and in the end the whole word), guided by the time-constraints of the graphemic presentation rate. During presentation, the whole word is projected faintly on the screen to allow anticipation (cf., Legge, Mansfield, & Chung, 2001). During practice, specific letter-speech sound mappings or groups of mappings (e.g., all long vowels such as 'maan' (moon), 'been' (leg), 'rook' (smoke)), similar to those addressed during instruction were presented. Practice is adjusted to the individual rate of acquisition by adapting time-constraints to the level of the child's performance.

2.5. Brain potential measurement

2.5.1. EEG recording and equipment

The EEG recording took place in a video-monitored and sound-proof room with temperature regulated by an air-conditioning system. There was no exposure to sunlight and the lighting of the room allowed a uniform and glare-free illumination. Participants and lab assistants were together at all times in the room while the experimenter was in an adjacent room, monitoring the EEG recording, stimuli presentation and the child's performance. Children were seated at approximately 80 cm distance from the computer screen and the lab assistant sat behind at a distance that safely avoided any possible distraction or interference on the visual field of the participant. Response buttons were placed on both arms of the child's chair.

The brain potential data were collected using a 64 channels Biosemi ActiveTwo system (Biosemi, Amsterdam, Netherlands). EEG was recorded DC (low-pass: 5th order sync digital filter) with a 1024 Hz sample rate. The Biosemi system uses two additional electrodes (Common Mode Sense [CMS] and Driven Right Leg [DRL]) located to the left and right of POZ, respectively, as recording reference and ground (see www.biosemi.com/faq/cms&drl.htm for details). The 64 electrodes were distributed across the scalp according to the 10–20 International system and applied using an elastic electrode cap (Electro-cap International Inc.). Electrode sites across the scalp are presented in Fig. 2 and the electrodes used in the analyses are highlighted. In addition, six external Flat-Type Active electrodes were used, four of which recorded vertical and horizontal electro-oculogram (EOG) and two were placed at mastoids for off-line reference.

2.5.2. Stimuli

Strings of words and symbols were used in the experiment. 80 bi-syllabic Dutch words were selected using estimates of age of acquisition (AOA). Estimates of AOA were based on two published

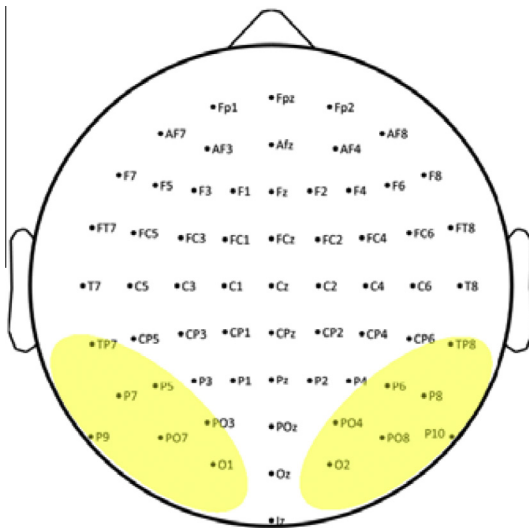


Fig. 2. Electrode sites across the scalp used in the current study. Electrodes included in the analysis (O1–O2, P07–P08, P03–P04, TP7–TP8, P9–P10, P7–P8, P5–P6) are indicated by highlighting.

ratings; (1) vocabulary estimates of 6-year-olds (Schaeplaekens, Kohnstamm, & Lejaegere, 1999), (2) AOA of Dutch words (Ghyselinck, Custers, & Brysbaert, 2004), and a subsequent student/parent familiarity rating of the selected words. The current selection criterion was motivated by a study indicating that AOA is a more sensitive index of lexical familiarity than either word frequency or neighborhood density when examining developmental change in visual word recognition (Garlock, Walley, & Metsala, 2001). Short strings contained 4 or 5 letters and long strings contained 6 and 7 letters. 80 symbol strings were created by converting the previous words into a special font: “3elementSymbols-1600” (P.L. Cornelissen, personal communication October 2011) with a similar number of line elements and comparable spatial frequency and contrast characteristics to actual letters (Pammer, Lavis, Hansen, & Cornelissen, 2004). For example, the word ‘molen’ (mill) became ‘molen’ in our symbol font. To avoid symbols resembling the fixation cross, the letters ‘z’ and ‘y’ (z and y) were replaced by ‘s’ and ‘u’ in the symbol strings.

All stimuli were presented at the center of the screen with a visual angle subtending on average $1.5^\circ \times 6.4^\circ$ (height \times width), using the lower case font “Arial” in white on a black background, at a font size of 40 and bold. They were presented for 700 ms and followed by a 1350 ms inter-stimulus interval (ISI) during which a white centered fixation cross was displayed. The stimuli were presented using an ASUS VW22U (resolution 1680×1050) monitor with a Dell Optiplex 760 dual-core 3.0 GHz computer and an ATI HD 6570, 2 Gb graphic card. The software used to present the stimuli was Presentation (Version 14.4, www.neurobs.com).

2.5.3. Task and procedure

The experiment had a 2×2 design, with the experimental conditions String Length (short vs. long) and String type (word vs. symbol). Children received 8 trial blocks; 4 word and 4 symbol blocks, alternating pseudo-randomly across participants. Short and long strings were presented in separate blocks. Trial blocks consisted of 44 trials, including 4 target trials (i.e., immediate repetitions). The presentation of the targets was pseudo-randomized to avoid consecutive presentations of targets. Children were instructed to press a button when they detected a repetition (i.e., when a string was immediately followed by itself). An example

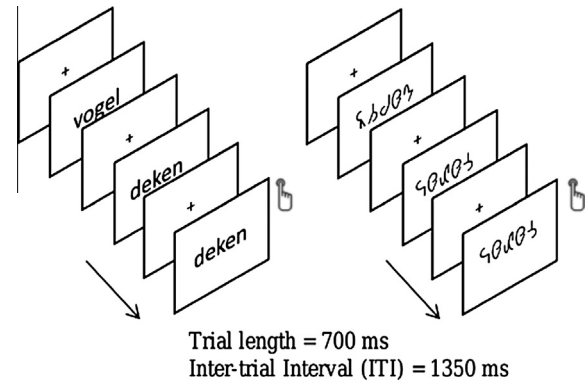


Fig. 3. An illustration of the word and symbol strings used in the present study. Children were required to attend to the strings and to press a button whenever a string was identical to its immediate predecessor. Strings of words and letter-like symbols were presented in a block design. A fixation cross was presented in between strings.

of the stimuli used and a schematic of the design are shown in Fig. 3.

The experiment lasted around 16 min including breaks. It was part of a longer experimental session consisting of two experiments (the duration was around 2 h, including electrode montage, instruction, and debriefing). The current experiment was scheduled following the first part of the other experiment, which lasted approximately 25 min. There were short pauses between trial blocks and longer breaks (around 5 min long) between experiments. The length of these pauses and breaks varied according to the needs of the child and all of them received a present at the end of the experimental session.

2.5.4. EEG preprocessing

All EEG data were preprocessed and analyzed with EEGLAB v.11.0.0.0b (Delorme & Makeig, 2004), an open source toolbox for Matlab (Mathworks, Inc.). When imported to EEGLab, the data were referenced to average mastoids, digitally filtered using a basic FIR filter (high pass 1 Hz and low pass 70 Hz), resampled to 256 Hz and epoched (from -500 to 1550 ms after stimulus onset). The baseline of each epoch was then corrected to remove residual activity differences prior to stimuli. Thus, the mean prestimulus activity (from -500 to 0 ms) was subtracted from the waveform for each channel and epoch.

Artifact removal was done in two steps. The first step consisted of visual inspection of the epochs to remove those epochs containing non-stereotyped artifacts such as head or muscle movements. Secondly, an Independent Component Analysis (ICA) was run using the ‘runica’ algorithm available in EEGLab (Makeig, Jung, Bell, Ghahremani, & Sejnowski, 1997). The extended option was used to perform a version of the infomax ICA algorithm (Lee, Girolami, & Sejnowski, 1999) that results in a better detection of sources with sub-Gaussian distribution, such as line current artifacts and slow activity. The resulting 64 ICA components were pruned by visual inspection of their scalp map, time course, mean activity and power spectra, in order to remove components related to artifacts such as line noise, eye blinks and eye movements. Components were classified as EEG activity according to the following criteria: scalp topography indicating an underlying dipolar source; spectral peaks typical of EEG; and a regular occurrence across single trials. The selection of independent components to reject was discussed between two investigators to increase reliability. The data was then reconstructed on an average (SD) of 34.75 (4.73) ICA components in the typical readers group. In the dyslexic group the averages of ICA components kept for pre- and posttest, were

33.83 (8.05) and 29.83 (7.59) components, respectively. Other EEG studies using this approach for data cleaning rejected up to 50–60% of the components (Bonte, Valente, & Formisano, 2009; Lenartowicz et al., 2014). Furthermore, spline interpolation was applied to channels with excessive artifacts (Perrin, Pernier, Bertrand, & Echallier, 1989). Pretest data from P10 and P9 were interpolated for three participants, from PO4 for two participants, and from O1 and O2 for one participant each; posttest data from PO3 was interpolated for five participants and from PO4 for one participant.

After artifact removal by ICA a new baseline correction (–500 to 0 ms) was done to avoid changes in the absolute EEG values after component rejection (Nolan, Whelan, & Reilly, 2010). Afterwards, data were low-pass filtered to 30 Hz (48 dB/octave) and re-referenced to the average of the 64 scalp electrodes (e.g., Maurer et al., 2007). Trials with responses (i.e., target trials and false alarms) were not included in the statistical analysis. The mean (SD) number of trials included in the analysis (after removal of artifacts and response epochs) in the typical readers group, for short words, long words, short symbols and long symbols were 78.95 (1.79), 78.95 (1.27), 73.90 (3.40) and 73.2 (4.11), respectively. The mean (SD) number of trials included in the analysis in the dyslexic group at pretest for short words, long words, short symbols and long symbols were 77.22 (4.57), 75.33 (4.54), 72.94 (4.71) and 70.50 (8.54) respectively; at posttest they were 79.39 (0.78), 78.78 (1.44), 75.50 (2.41) and 72.61 (5.37) respectively. Finally, individual subject averages were calculated for each experimental condition.

The N170 peak of the brain potential elicited by the visual strings was detected in the electrodes of interest (see Section 2.5.1) by searching for the maximum amplitude value within the time window of 175–300 ms based on our previous study and on visual inspection of the current data. The N170 peak amplitudes (μV) and latencies (ms) were subjected to statistical analyses performed using the SPSS Statistics 22 software package (IBM Corp., Armonk, NY). For all analyses Greenhouse-Geisser correction of degrees of freedom was used to calculate p values when the assumption of sphericity was violated.

3. Results

3.1. Behavioral results

For all analyses, standardized scores were used instead of raw scores, in order to assess the child's position within the distribution of a normative sample. Due to reduced variance, no reliable norm scores were available for the accuracy measures of the three sub-tasks of the 3DM word reading. Hence, raw scores were used for these measures. The behavioral results are presented in three sections. First, we will present the differential patterns of pretest measures for dyslexic children and typical readers. Second, we will assess changes in the pattern of pretest measures associated with training. Finally, we will examine individual differences in the group of dyslexic children with regard to their sensitivity to the training. This analysis will differentiate improvers vs. non-improvers.

3.1.1. Pretest measures

The results of the ANOVAs performed on the pretest data in reading accuracy and speed measures are shown in Table 1. The table shows a deficit in dyslexics that is mainly manifested in measures of reading fluency. The dyslexic group attained reasonably high levels of reading accuracy, albeit significantly lower than those of the typical readers. With regard to the letter-speech sound measures (i.e., the scores on the letter-speech sound (LSS) mapping tasks of the 3DM), only the fluency score associated with letter-speech sound identification discriminated between groups.

3.1.2. Reading gains

To examine changes in the pattern of pretest measures associated with training, a repeated-measures ANOVA was performed on the pre- and posttest data of the dyslexic group with within-subjects factor *Training* (2 levels: pre- and posttest). The results of this analysis are presented in Table 2. The table shows significant gains after training for the main word reading measures. The training effects were less marked for accuracy measures, as it might be expected given the relatively high accuracy scores at

Table 2

Results of repeated measures ANOVA in dyslexics ($n = 18$) with training as within-subjects factor.

	Pretest	Posttest	ANOVA		
	M (SD)	M (SD)	F	p -value	η^2
<i>3DM Word reading - accuracy^a</i>					
High frequency	92.02 (7.20)	96.48 (7.15)	6.56	0.046	0.28
Low frequency	82.96 (16.54)	91.12 (12.59)	9.71	0.019	0.36
Pseudowords	70.72 (16.37)	78.33 (19.19)	2.61	0.166	0.13
Total [T] ^b	32.33 (12.76)	40.72 (14.10)	7.88	0.032	0.32
<i>3DM Word reading - fluency [T]</i>					
High frequency	30.50 (5.43)	35.67 (7.41)	29.76	0.000	0.64
Low frequency	31.11 (6.46)	34.89 (6.94)	19.58	0.000	0.54
Pseudowords	30.78 (5.55)	32.89 (7.37)	3.73	0.112	0.18
Total	29.83 (5.53)	33.89 (7.15)	22.58	0.000	0.57
<i>One-Minute Test -fluency [SS]^c</i>					
Text reading - fluency[T]	33.11 (5.66)	34.61 (6.36)	4.24	0.098	0.2
<i>Letter-speech sound associations [T]</i>					
LSS identification - accuracy	43.83 (13.27)	45.94 (8.63)	0.43	0.520	0.03
LSS discrimination - accuracy	45.72 (8.59)	47.67 (9.91)	1.10	0.331	0.06
LSS identification - fluency	46.00 (7.06)	49.22 (10.65)	2.15	0.198	0.11
LSS discrimination - fluency	51.83 (8.92)	55.11 (10.24)	2.78	0.166	0.14
3DM spelling - accuracy	36.11 (8.34)	44.33 (9.83)	19.21	0.000	0.53
3DM spelling - fluency	40.61 (8.30)	44.83 (10.90)	4.66	0.092	0.22

Note. LSS = Letter-speech sound.

False Discovery Rate (FDR) correction for multiple comparisons was applied to the p values.

^a Raw scores.

^b T scores ($M = 50$, $SD = 10$).

^c SS scores ($M = 10$, $SD = 3$).

Table 3

Descriptive statistics of reading scores in dyslexics improvers and non-improvers.

	Improvers	Poor Improvers	ANOVA		
	<i>M</i> (<i>SD</i>)	<i>M</i> (<i>SD</i>)	<i>F</i>	<i>p</i> -value	η^2
<i>N</i>	9	9			
Sex ratio (m:f)	3:6	5:4			
Handedness (L:R)	1:8	2:7			
Age	9.13 (0.34)	8.97 (0.57)	0.51	0.484	0.03
3DM Word reading – accuracy ^a					
High frequency	91.93 (6.81)	92.11 (7.98)	0.00	0.960	0.00
Low frequency	85.85 (13.83)	80.07 (19.27)	0.53	0.476	0.03
Pseudowords	69.64 (13.71)	71.80 (19.47)	0.07	0.788	0.01
Total [T] ^b	31.11 (12.62)	33.56 (13.54)	0.16	0.697	0.01
3DM Word reading – fluency [T]					
High frequency	30.56 (4.77)	30.44 (6.31)	0.00	0.967	0.00
Low frequency	31.89 (6.31)	30.33 (6.89)	0.25	0.624	0.02
Pseudowords	30.00 (5.52)	31.56 (5.79)	0.34	0.568	0.02
Total	29.56 (5.36)	30.11 (6.01)	0.04	0.839	0.00
One-Minute Test –fluency [SS] ^c	3.89 (1.76)	3.00 (1.87)	1.08	0.315	0.75
Text reading – fluency [T]	34.78 (4.99)	31.44 (6.06)	1.62	0.221	0.71
Letter-speech sound associations [T]					
LSS identification – accuracy	43.11 (11.75)	44.56 (15.33)	0.05	0.825	0.00
LSS discrimination – accuracy	46.78 (8.83)	44.67 (8.73)	0.26	0.617	0.02
LSS identification – fluency	46.11 (6.85)	45.89 (7.69)	0.00	0.949	0.00
LSS discrimination – fluency	49.33 (10.69)	54.33 (6.38)	1.45	0.246	0.08
3DM spelling – accuracy [T]	38.00 (9.68)	34.22 (6.78)	0.92	0.352	0.05
3DM spelling – fluency [T]	41.44 (9.74)	39.78 (7.08)	0.17	0.683	0.01
Phoneme deletion –accuracy [T] ^d	40.88 (8.44)	37.44 (10.38)	0.55	0.470	0.04
3DM naming speed scores [T] ^d					
Letters	37.13 (6.36)	37.89 (9.12)	0.04	0.846	0.00
Numbers	37.88 (8.77)	35.33 (8.75)	0.36	0.559	0.02
Total	34.25 (8.26)	36.00 (10.58)	0.14	0.712	0.01

Note. LSS = Letter-speech sound.

^a Raw scores.^b T scores (*M* = 50, *SD* = 10).^c SS scores (*M* = 10, *SD* = 3).^d Data missing for one participant; Improvers *n* = 8.

pretest. The training effect was most marked for reading fluency measures, with the exception of the fluency measures derived from the 3DM pseudowords task and the One-Minute test where the gains in standardized scores did not reach significance. Finally, with regard to the tasks related to letter-speech sound mapping, the dyslexic children showed gains in spelling accuracy scores.

3.1.3. Individual differences in reading improvement

Participants were classified as improvers or non-improvers based on the median of the post-pretest difference in the standardized total fluency score for the 3DM word reading task (Vellutino & Scanlon, 1996). The normative scores were T scores where 50 is the mean and 10 the standard deviation. The total 3DM word reading fluency score was used, as it is a reliable and sensitive measure, which is part of a test battery widely used for diagnostic assessment of dyslexia in the Netherlands (see Section 2.3). Control analyses were performed comparing improvers and non-improvers at pretest to confirm that the groups did not differ in their reading scores before the training. The results of these analyses are presented in Table 3.

The individual differences in reading fluency are plotted in Fig. 4. The median of the differences in T scores was 3.50; the mean (SD) difference was 4.06 (3.63), range 0–11. The ANOVAs including *Improvement* as a between-subjects factor, revealed that improvers and non-improvers did not differ in their initial reading scores, *ps* > 0.221 (see Table 3).

3.1.4. Experimental task performance

For the sake of completeness, we report the outcomes of analyses of group differences and training effects with regard to the

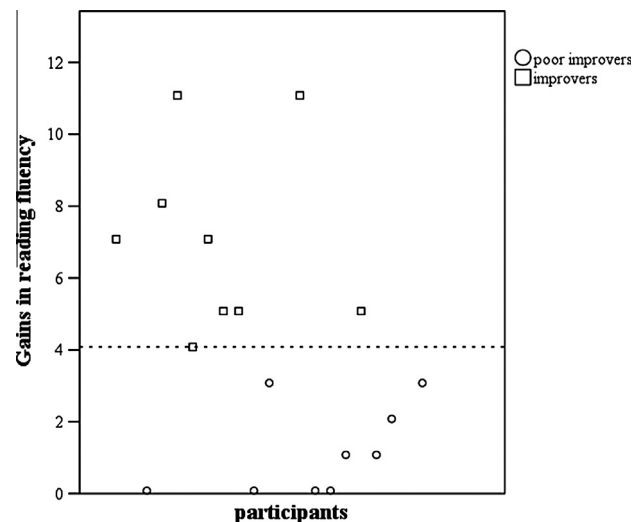


Fig. 4. Individual differences in the gain in reading fluency (3DM standardized total score) in the dyslexic group (*N* = 18). The dashed line refers to the group median used to classify subjects as improvers or non-improvers.

accuracy and latency measures obtained from the experimental task. The results of the analyses on the data from the experimental task are presented in the Appendix A. In brief, accuracy was lower and false alarm rate were higher in the dyslexic children relative to the typical readers and these group differences were not affected by training. The reaction times did not discriminate between groups.

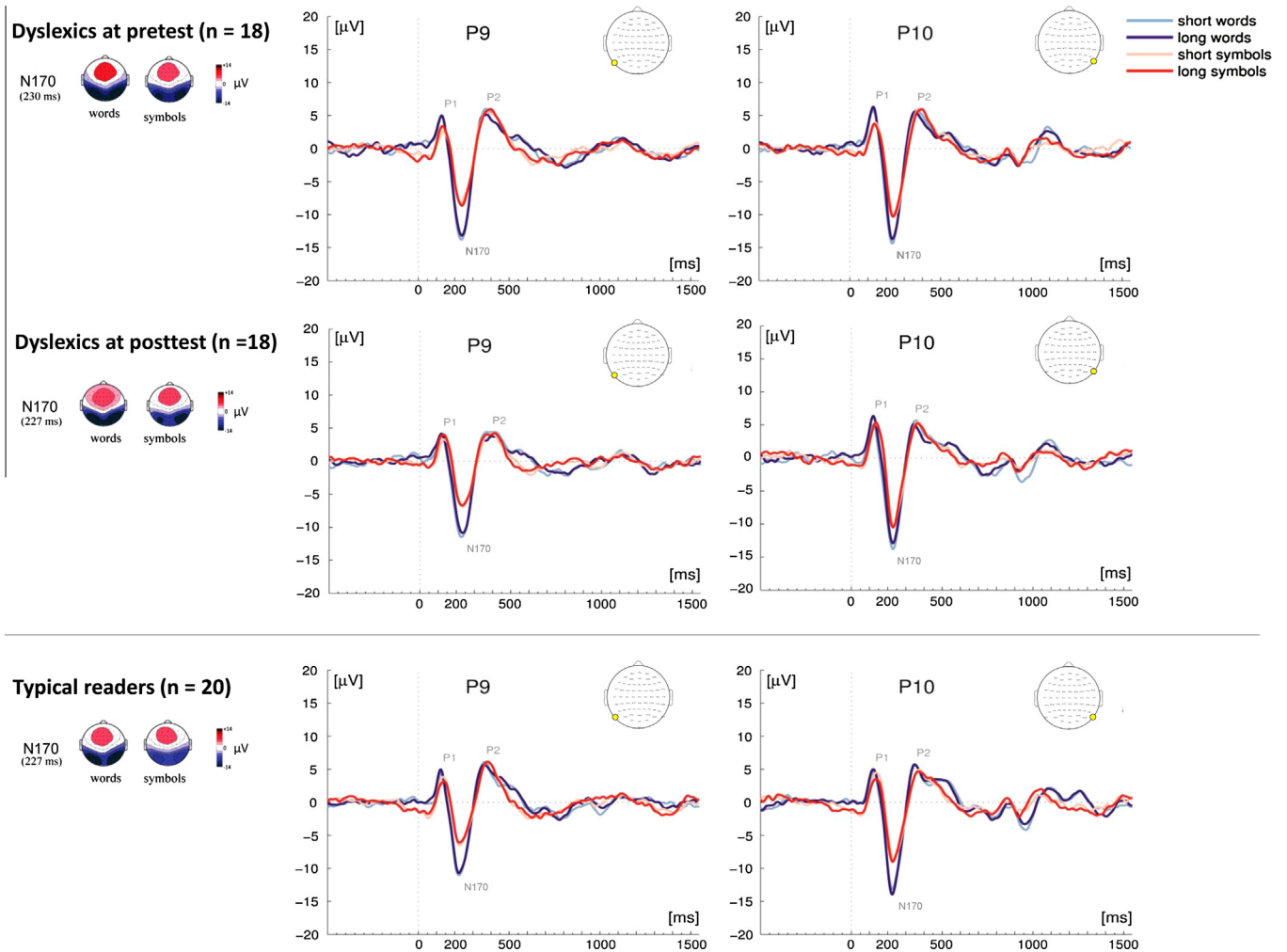


Fig. 5. Group ERPs to word and symbol stimuli at P9 and P10. Topographical maps showing the course of neural activity following stimulus onset. Posterior activations and polarity are visible at peak latencies (group mean latencies).

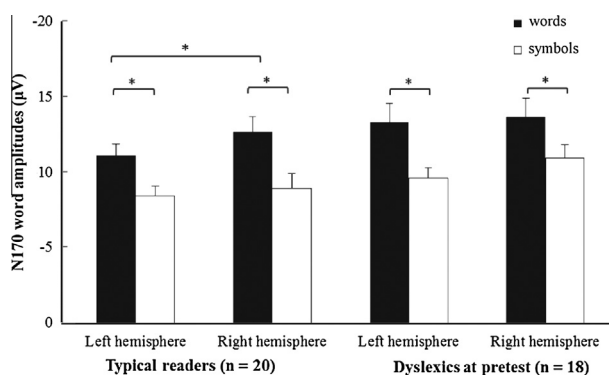


Fig. 6. Mean N170 amplitude to words at left and right hemisphere sites in dyslexics in the pretest and typical readers (pretest only). Left hemisphere amplitudes are averaged across TP7, P9, P7, P5, PO7, PO3 and O1 sites, and right hemisphere across their homologue pairs. Error bars show standard errors of the sample.

3.2. Brain potential results

Fig. 5 shows the ERPs and their scalp distribution (at mean peak latency for each group) for dyslexic and typical readers at pre- and posttest. N170 amplitudes discriminated between words and symbols in both groups and in dyslexic children at both pre- and

posttest. Although our focus was on amplitudes, the analyses on N170 latencies have been included as [Appendix B](#). We included summary tables of the main statistical analyses on N170 amplitudes as well as P1 and P2 components in [Appendix C](#).

3.2.1. Pretest

Our previous brain potential study showed that N170 amplitudes for words were reduced at the left compared to the right hemisphere sites in typical readers but not in dyslexics (Fraga González et al., 2014). We examined whether the same group difference was present using the current sample of dyslexics. A mixed-model ANOVA was performed on the data of dyslexics and typical readers at pretest, including the between subjects factor Dyslexia. The within-subjects factors were String Type (2 levels: words or strings of letter-like symbols), String Length (2 levels: short or long strings), Hemisphere (2 levels: right and left hemisphere) and Electrode (7 levels. Electrodes pairs at occipital, occipito-temporal and parietal locations were included; O1-O2, PO7-PO8, PO3-PO4, TP7-TP8, P9-P10, P7-P8, P5-P6). A follow-up analysis on pretest data of the dyslexics examined the specific pattern of responses in dyslexics.

The current mixed-model ANOVA performed on N170 amplitudes revealed a significant three-way interaction effect including Dyslexia, Hemisphere and String Type, $F(1,36) = 5.76$, $p = 0.022$, $\eta^2 = 0.14$. This interaction is shown in Fig. 6. Follow-up analyses

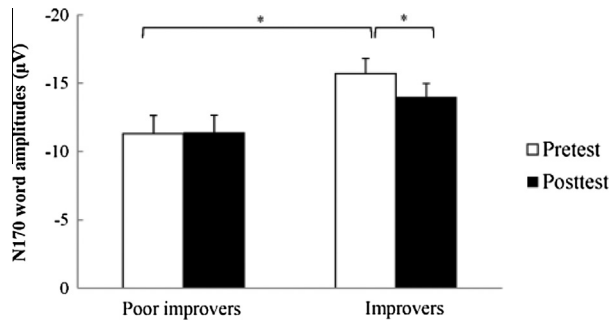


Fig. 7. Mean N170 amplitudes for words averaged across all electrode pairs (O1-O2, PO7-PO8, PO3-PO4, TP7-TP8, P9-P10, P7-P8, P5-P6) for non-improvers and improvers. Open bars refer to pretest N170 amplitudes for words and filled bar to posttest amplitudes.

were done on the data of each group separately. These analyses revealed that N170 amplitude to words in the typical readers was smaller over the left than right hemisphere, $F(1,19) = 4.49$, $p = 0.048$, $\eta^2 = 0.19$, while lateralization was absent for the N170 amplitude to symbols, $p > 0.512$. In dyslexic readers, lateralization of N170 amplitude for both symbols and words was absent, $ps > 0.208$. Collectively, this pattern replicates the findings reported previously.

3.2.2. Posttest

To assess the effects of Training on N170 amplitude, we performed a repeated-measures ANOVA on the data of the dyslexic children with Training (2 levels; pre- vs. posttest) added to the within-subjects factors String Type, String Length, Hemisphere and Electrode. The analysis indicated that the effect of Training just failed to reach an acceptable level of significance, $ps > 0.077$.

3.2.3. Differential responsiveness

In order to account for individual differences in responsivity to training, we performed a mixed-model ANOVA with the between-subjects factor Improvement (with 2 levels: improvers and non-improvers, as classified by a median split on their reading gains, see Behavioral Results). The within-subject factors were those of the previous analysis (i.e., Training, String Type, String Length, Hemisphere and Electrode). The analysis revealed a significant interaction effect between the factors Training, String Type and Improvement, $F(1,16) = 6.21$, $p = 0.024$, $\eta^2 = 0.28$. All other effects including the factor Training were not significant, $ps > 0.082$. Subsequently, we performed repeated-measures ANOVA on the data of improvers and non-improvers, separately.

The analysis done on the data of the improvers yielded a significant interaction, including the factors String Type and Training, $F(1,8) = 7.51$, $p = 0.025$, $\eta^2 = 0.48$. The follow-up analysis performed on N170 amplitudes for words revealed a significant main effect of Training, $F(1,8) = 7.30$, $p = 0.027$, $\eta^2 = 0.48$, indicating reduced N170 amplitudes across both hemispheres for the posttest relative to the pretest. This result is shown in Fig. 7. The mean (SD) amplitude for words at pre- vs. posttest were 15.70 (3.36) μV and 14.01 (2.87) μV , respectively. The analysis on the data obtained from non-improvers failed to reveal a main effect of Training or an interaction including Training and String Type, $ps > 0.117$.

3.2.4. Relation to fluency gains

We examined whether the training-related change in N170 amplitude to words was associated with individual differences in fluency gain. The analysis focused on N170 amplitudes recorded from the left-hemisphere sites that were most responsive to training based on visual inspection of the averages at pre- and posttest.

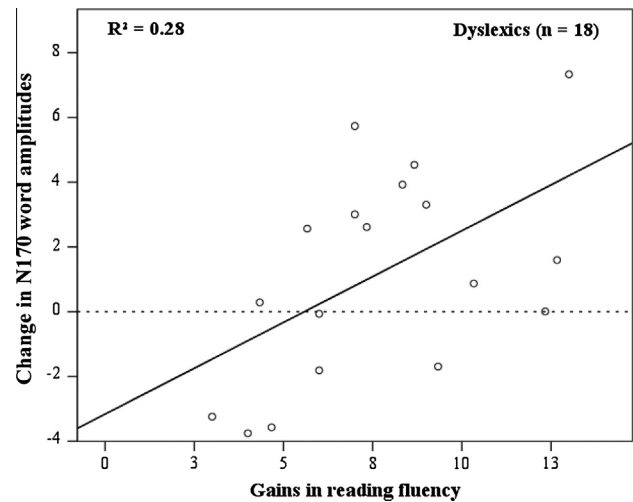


Fig. 8. Linear regression between post-pretest change in N170 amplitudes to words at the left posterior electrodes (average of P9, P7, PO7 and O1) and gains in reading fluency (average of 3DM high and low frequency word reading and One Minute test). A change towards positive values along the y-axis refers to a decrease in N170 amplitude.

(P9, P7, PO7 and O1). These sites showed a more pronounced String Type effect, compared to other sites, in the pretest comparisons in both dyslexics as well as typical readers. The training-related change in N170 amplitude was averaged across sites and then included in a regression analysis relating N170 amplitude to a composite score of reading fluency. The composite score of reading fluency was computed by averaging the raw scores of the One-Minute Test and the 3DM word reading tasks of high and low frequency (single).

The analysis showed a significant relation between training-related N170 amplitude change at the selected left-hemisphere sites and fluency gain, $R = 0.53$, $R^2 = 0.28$, $\beta = -0.49$, $t = -2.49$, $p = 0.024$, plotted in Fig. 8. It can be seen that the training-related decrease in N170 amplitude is associated with a gain in reading fluency. A similar analyses performed on N170 amplitudes for words recorded from the right hemisphere or N170 amplitudes to symbol strings at left and right hemisphere sites yielded non-significant outcomes, $p = 0.177$, $p = 0.134$ and $p = 0.229$, respectively.

3.2.5. N170 amplitude as predictor

To assess whether N170 amplitude at pretest would discriminate between children who benefit from the training (improvers) vs. those who do not (non-improvers), we performed a mixed-model ANOVA on the pretest N170 amplitude data of the dyslexic children with Improvement as a between-subjects and the same within-subject factors as in previous analyses (String Type, String Length, Hemisphere and Electrode). The analysis yielded a significant main effect of String Type, $F(1,16) = 37.42$, $p < 0.001$, $\eta^2 = 0.70$, indicating larger amplitudes for words vs. symbol strings in both groups, which was included in a significant interaction with Improvement, $F(1,16) = 7.51$, $p = 0.015$, $\eta^2 = 0.32$. Subsequently, we performed separate analyses on N170 amplitudes to words and symbol strings. The analysis for words yielded a significant main effect of Improvement, $F(1,16) = 6.34$, $p = 0.023$, $\eta^2 = 0.28$, indicating larger word N170 amplitudes in improvers relative to non-improvers across both hemispheres (see Fig. 7). The mean (SD) N170 amplitudes to words at pretest were 15.70 (3.36) μV for improvers and 11.30 (4.01) μV for non-improvers. The analysis for symbol strings did not result in significant outcomes, $ps > 0.234$.

Additionally, we performed a discriminant-function analysis to further assess how accurately N170 responses could classify participants as improvers vs. non-improvers. The grouping variable was *Improvement* and the N170 amplitude for words at pretest (averaged across electrodes) was included as independent variable. The analysis yielded a significant outcome, Wilk's Lambda $F(1, 16) = 6.34, p = 0.023$. The canonical correlation was 0.53, eigenvalue = 0.40. For the non-improvers group, 6 of the 9 subjects were correctly classified (66.67% accurate) and for the improvers group, 7 of the 9 subjects were correctly classified (77.78% accurate).

4. Discussion

The current study yielded three major findings. First, the training aimed at improving reading fluency resulted in significant fluency gains in dyslexic children although they did not attain the level of reading fluency seen in typical readers. Secondly, The N170 amplitude associated with word recognition was altered by the training. More specifically, the N170 amplitude decreased from pre- to posttest. Moreover, the N170 amplitude decrease associated with training at the left hemisphere was related to the gain in reading fluency. Importantly, the pattern of change in N170 amplitude was observed only for dyslexic children who demonstrated reading fluency gains (improvers). The pattern of change in N170 amplitude was absent in dyslexic children who did not respond to the training (non-improvers). Finally, N170 amplitude at pretest differentiated between improvers and non-improvers; that is, N170 amplitude to words at pretest was larger in improvers than non-improvers, whereas group differences were not seen in the reading scores.

At pretest, the reading scores of the dyslexic children revealed that reading fluency was their primary deficit. In addition, the comparison between the dyslexic and typical readers showed that N170 amplitude to words was left-lateralized for typical readers, with smaller N170 amplitudes over the left compared to the right hemisphere whereas hemispheric differences were absent for dyslexic children. This pattern of findings is consistent with the results reported in a previous study (Fraga González et al., 2014). The relatively enhanced N170 amplitude over the left hemisphere in dyslexic children relative to the typical readers was interpreted to suggest that dyslexics had to invest greater effort in the visual decoding of words. It was suggested that the allocation of more effort to words is likely to result in a more pronounced activation of the VWFA, thus enhancing N170 amplitude to words in dyslexics. More specifically, it was argued that dyslexic children may have relied more strongly than typical readers on orthographic aspects of words. This suggestion would be compatible to previous findings (Ruz & Nobre, 2008), indicating that allocating more effort to orthographic aspects elicits larger N170 amplitudes relative to the processing of phonological or semantic aspects (cf. Fraga González et al., 2014; p. 12).

The pre- vs. posttest comparison showed that training had a beneficial effect on reading fluency. The current findings are consistent with our previous study using the same training procedures and pattern of outcome measures (Fraga González et al., 2015). The joint pattern of findings converges in showing that relatively small but significant gains in reading accuracy together with more substantial improvements in reading fluency, as assessed by the 3DM fluency scales but not when the scores on the *One Minute Tests* are taken as outcome measure. Most likely, the current failure in detecting fluency gains using the *One Minute Test* is due to lack of power. In the previous study, we observed a trend towards a gain in fluency, albeit not significant (Fraga González et al., 2015), while Tijms (2007) reported a substantial gain in reading

fluency using a large sample of dyslexic children ($n = 140$ compared to the current $n = 18$).

In spite of a significant gain in reading fluency, it should be noted that, after a half year of intensive training, the dyslexic children did not attain the proficiency levels seen in typical readers (35.67 vs. 52.95, respectively on the 3DM fluency scale for frequent words). In a series of studies, Tijms and colleagues examined the time course of reading fluency during and following a training similar to ours (e.g., Tijms, 2007, 2011; Tijms, Hoeks, Paulussen-Hoogeboom, & Smolenaars, 2003). These studies showed that the beneficial effect of training consisted initially of gains in reading accuracy while improvements of reading fluency lagged behind. Thus, the largest gain in reading accuracy was observed following the first six months of training and then levelled off during the remaining 6 months of the training and follow-up (1–4 years). In contrast, reading fluency continued to improve during the second half of the training and into the follow-up period (Tijms, 2007). The protracted time course of gains in reading fluency was interpreted to suggest that training allowed for the development of explicit and systematic word decoding skills that are then driving self-teaching mechanisms bootstrapping fluent reading (cf. Tijms, 2007; p. 890). It would be of considerable interest to examine whether N170 amplitude to words would parallel the time course of gains in reading fluency during treatment and follow-up.

The pre-vs. posttest comparison for N170 amplitude to words did not reach an acceptable significance level when considering the full sample of dyslexic children. It did, however, when responsiveness to training was taken into account. Improvers showed a decrease in N170 amplitude to words following training. Such a decrease was absent for non-improvers. The training-related decrease in N170 amplitude to words in improvers could be interpreted to suggest that, in line with the notion relating N170 amplitude to the amount of effort invested in visual word decoding, training reduced the need for allocating effort to word decoding. This interpretation is compatible with the results of previous studies showing normalization of neural activity in responders relative to poor responders to intervention (Davis et al., 2011; Molfese et al., 2013; Odegard, Ring, Smith, Biggan, & Black, 2008; Simos et al., 2007).

At this point, it should be noted that, although the pattern of N170 amplitude in improvers changed towards the N170 amplitude pattern seen in typical readers, it did not left-lateralize as in typical readers. Thus, neural abnormalities continue to exist in improvers. This observation is consistent with the behavioral results showing that, despite significant gains in reading speed, reading fluency in improvers did not attain the level of proficiency seen in the typical readers. Previous studies indicated that N170 lateralization may depend on the degree of effort that is allocated to word reading. For example, Okumura and colleagues observed that N170 amplitude is not lateralized when stimuli are task irrelevant while N170 amplitude did lateralize when more effort was required (Okumura, Kasai, & Murohashi, 2014, 2015). Similarly, fMRI studies showed that lateralization of word reading critically depends on task difficulty (Cohen, Dehaene, Vinckier, Jobert, & Montavont, 2008) or attentional characteristics of the word-reading task (Yoncheva, Wise, & McCandliss, 2015). Collectively, these studies suggest that, besides VWFA specialization for reading, attention and decoding strategies have a significant impact on the lateralization and strength of N170 responses.

One comment is in order here. At pretest, N170 amplitude to words in responders was larger than in typical readers and non-responders. Thus, a training-related decrease in N170 amplitude moves responders towards both typical and non-responder values. This seemingly counter-intuitive pattern might be interpreted by referring to the notion of an inverted U-shaped development of visual expertise in which perceptual learning becomes highly

important during the first two or three years of learning to read and then gradually declines as expertise develops (e.g., Maurer et al., 2011; Hasko, Bruder, Bartling, & Schulte-Körne, 2012). Given that N170 amplitude to words is a neural manifestation of visual expertise, the dyslexic readers might be positioned at the up-going flank of the inverted U-shaped curve of visual expertise while the typical readers are positioned at the down-going flank. The difference in N170 amplitude between improvers and non-improvers is then explained by assuming that, relative to improvers, the non-improvers are positioned lower at the up-going flank of the visual expertise curve. We will come back to this issue when discussing the merits of N170 amplitude as a potential neural marker of training sensitivity.

The current results indicated that training-related changes in N170 amplitude for words at the left hemisphere were related to gains in reading fluency. Although the strength of the correlation is low, the current observation and the dissociation between hemispheres for this effect, is important as it provides support for the validity of N170 as a neural correlate of reading expertise. N170 amplitudes recorded over the left occipito-temporal brain regions are proposed to reflect the activity of the VWFA, which specializes for fast word recognition during learning to read (Dehaene, Cohen, Morais, & Kolinsky, 2015; McCandliss et al., 2003). The current association between a decrease in N170 amplitude over the left hemisphere and improvements in reading fluency provides support for the notion of an inverted U-shaped development of visual expertise (e.g., Maurer, 2006).

It is important to emphasize that the focus of the current training was on automation of letter-speech sound associations. Hence, the training is expected to directly influence the parieto-temporal system responsible for multisensory integration. Previous research suggested that the multimodal association system for reading supports the specialization of visual areas (Sandak et al., 2004; Schlaggar & McCandliss, 2007). Accordingly, studies reported that specialization of occipito-temporal areas to print was absent in kindergarten (Brem et al., 2010) but becomes apparent once children learn grapheme-phoneme correspondences (Maurer & McCandliss, 2007). The present results are in line with such an interactive account, as our training modulated visual N170 responses at the proximity of the VWFA (see also Yoncheva et al., 2015).

A final major finding of the present research was that N170 amplitude to words discriminated between improvers vs. non-improvers at pretest while reading measures did not differ between groups. More specifically, N170 amplitudes in non-improvers were smaller relative to improvers. The current finding is consistent with the results of a previous MEG study by Rezaie et al. (2011a). That study reported under-activation of the ventral occipito-temporal areas in struggling readers who failed to benefit from an intervention in middle school compared to those who were being helped (see also Molfese et al., 2013; Rezaie et al., 2011b). It has been shown that visual responses emerging during the initial stages of reading acquisition decrease and left-lateralize as reading expertise develops (Maurer et al., 2006). The stronger visual responses during the initial stages of reading acquisition have been interpreted to suggest early perceptual learning and top-down predictions from phonological areas (Price & Devlin, 2011). In this regard, the initially smaller N170 amplitudes for words in non-improvers may indicate that they are lagging behind improvers or follow a different perceptual-learning trajectory. An alternative interpretation of the initial N170 differences between improvers and non-improvers relates to attentional strategies adopted during the task. That is, the initially larger N170 amplitudes in improvers may reflect the allocation of more attentional resources to orthographic processing that can be released once letter-speech sound mapping becomes automated.

Thus, a previous brain potential study reported that paying attention to orthographic cues may enhance early visual responses relative to when phonological cues are attended (Ruz & Nobre, 2008).

5. Study limitations

An apparent limitation of the current study is in order. The current design did not allow for disentangling the effects of training from those related to the passage of time. It should be noted, however, that the assessments of both improvers and non-improvers were at the same time points and, thus, can be assumed to be equally susceptible to the passage of time. Secondly, our findings regarding changes on N170 amplitudes were word specific and not found for symbol strings. It seems unlikely that general maturation effects would discriminate between string type. Furthermore, we presented high frequency words that are already well known to both typical readers and dyslexics. Hence, adaptation of neural responses to overlearned and already familiar stimuli within less than half a year do not seem a likely explanation for the observed changes in N170 amplitude (see also Maurer et al., 2005). Finally, it has been suggested that the most pronounced changes in visual responses take place during the earlier stages of reading acquisition, thus before the current age of our participants (Brem et al., 2010; Maurer et al., 2005; Price & Devlin, 2011).

6. General conclusions

In conclusion, the present study contributes to the literature suggesting the sensitivity of N170 amplitudes for words as a neural marker for reading fluency in dyslexia. First, we found differential training effects on N170 in the group of improvers compared to that of non-improvers. Secondly, we obtained an association between a left-lateralized decrease in N170 amplitudes and gains in reading fluency supporting the contribution of VWFA specialization. Thirdly, our findings indicated a dissociation between N170 amplitude and reading scores in discriminating between improvers and non-improvers at pre-test. The latter finding, in particular, illustrates the additional value of neural markers in predicting the acquisition of reading skills and/or individual differences in treatment responsiveness (Brem et al., 2013; Hasko et al., 2014; Lemons et al., 2010; Molfese et al., 2013). Collectively, the current pattern of results provides further support for the relation between N170 amplitude and reading expertise and its potential use in clinical studies.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.bandc.2016.05.001>.

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